

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/CZ2004/000017

International filing date (day/month/year)
30.03.2004

Priority date (day/month/year)
31.03.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/282

Applicant
PLIVA-LACHEMA A.S.

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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10/549296

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: US-A-6 136 336 (KUWAHARA ETSUHISA ET AL) 24 October 2000 (2000-10-24)
- D2: WO 99/61451 A (MISTR ADOLF ; LACHEMA AS (CZ); M & ECARON (CZ); POULOVA ANNA (CZ); ZAL) 2 December 1999 (1999-12-02)

If not indicated otherwise, the relevant passages are those mentioned in the International search report.

Art. 33(2) The present application meets the requirements of Article 33(2) PCT, because the subject-matter of **claims 1-19** appears to be new in the sense of Article 33(2) PCT.

The prior art cited in the search report does not disclose a pharmaceutical composition comprising the claimed compounds, a neutral saccharide and a modified polysaccharide in granules having a particle size below 0,5mm.

Art. 33(3) The subject-matter of **claims 1-19** is not considered to involve an inventive step in the sense of Article 33(3) PCT.

D2 discloses pharmaceutical compositions comprising platinum complexes according to the present application from which the subject-matter of **claims 1-19** differs in that no inclusion complexes with cyclodextrins are used (see the description of the present application, page 2, first paragraph).

The problem to be solved by the present invention may therefore be regarded as how to provide stable solid dosage forms of the claimed platinum complexes having a good solubility (see the description of the present application, page 2, second paragraph).

The present application suggests to solve the problem posed by granulating the active compounds with a neutral saccharide and a modified polysaccharide.

Yet, stable compositions in hard gelatin capsules comprising satraplatin, microcristalline cellulose and lactose are known from D1. Furthermore, D4 discloses how to reduce the particle size in order to improve solubility (milling/grinding of satraplatin in mixtures with different polymers).

Taking into account the teaching of the cited prior art the following reasoning applies:

With respect to the subject-matter of **claims 1-19** the applicant's attention is drawn to the fact that there seems to be no basis for inventive step within the present application as filed since no evidence can be found that the features which are novel result in a solution of the posed problem which could not have been foreseen by the skilled person.

Being aware of the teaching of D2 the skilled person performed an arbitrary choice out of one list containing all suitable excipients to select.

Since there is no surprising effect resulting from that choice, the solution proposed in claims of the present application is not considered to be inventive in the sense of Article 33(3) PCT.

It is therefore noted, that the solution proposed in **claims 1-19** of the present application is not considered to be inventive in the sense of Article 33(3) PCT.

Art. 33(4) The subject-matter of **claims 1-19** is considered to be industrially applicable in the sense of Art. 33(4) PCT.

Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
 translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-19
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-19
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	

2. Citations and explanations

see separate sheet